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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,919	PANACCIO ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,21 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,21 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response

1. Applicant's response filed on 5/2/05 is acknowledged and entered.

Status of claims

2. Claims 5-20, 22, 24-48 have been canceled.

Claims 1, 21 and 23 have been amended.

Claims 1-4, 21 and 23 are pending and under examination.

Claim Rejection - 35 U.S. C. 112, first paragraph moot

3. In view of cancellation of claims, the written description rejection and enablement rejection under U.S.C. 112, first paragraph are moot for claims 6, 17-20.

Claim Rejection - 35 U.S. C. 112, first paragraph withdrawn

4. In view of amendments to the claims, the rejections under U.S.C. 112, first paragraph for claims 21 and 23 are withdrawn for the recitation of an isolated or recombinant polypeptide having at least about 70% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1 or at least about 50% sequence identity to the amino acid residues1- 50 of SEQ ID NO: 1

Claim Rejection - 35 U.S. C. 112, first paragraph maintained for vaccine composition

5. The rejection of claims 21 and 23 under 35 U.5.C. 112, first paragraph while being enabling for an immunogenic composition comprising an isolated or recombinant *L. intracellularis* hemolysin polypeptide consisting of SEQ.ID.NO: 1 and one or more carriers, diluents or adjuvants suitable for veterinary or pharmaceutical use does not reasonably provide enablement for a vaccine composition comprising an effective amount of immunogenic component comprising an isolated or recombinant Lawsonia spp hemolysin polypeptide consisting of SEQ.ID.NO: 1 is maintained as set forth in the previous Office action.

The nature of the disclosed invention is preparing recombinant polypeptides from

L. intracellularis only. The invention is drawn to an isolated recombinant polypeptide consisting of the amino acid sequence SEQ ID NO: 1 which is encoded by *L. intracellularis* polynucleotide, SEQ.ID.NO: 2 (pALK12, ATCC 207195). The specification also teaches that this full-length protein contains 251 amino acids. The specification discloses the claimed could be used to identify *L. intracellularis infection* and as an immunogen and formulating the compositions in Freund's adjuvant to immunize mice for preparing antibodies. However, the specification provides no information on all Lawsonia spp (now present and the newly discovered species) and the protective immunogenicity of the claimed composition for prophylaxis (i.e., protecting) or treating the animal from infection. The specification also fails to teach that the claimed composition alone or in combination with adjuvants or carriers provides protection against infection in any acceptable animal model. Vaccines by definition trigger an immunoprotective response in the host vaccinated and mere antigenic response is insufficient to provide for enablement of vaccines. This specification fails to teach protective immune response generated by said isolated polypeptide vaccine. It is well recognized in the vaccine art, that it is unclear whether an antigen(s) derived from a pathogen will elicit protective immunity. Ellis, R.W. (Chapter 29 of "VACCINES" [Plotkin, 5.A. et al. (eds) published by W. B. Saunders company (Philadelphia) in 1988, especially page 571, 2nd full paragraph] exemplifies this problem in the recitation that "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.... and thus protect the host against attack by the pathogen". The specification fails to teach the claimed composition confer protection against infection, as is requisite of a vaccine composition. The courts have held that it is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute adequate enablement. (*Genentech Inc. v. Novo Nordisk A/5 Ltd., 42 USPQ2d 1001*). Moreover, the specification must have been enabling at the time the invention was made-and developments after the time of filing are of no consequence to what one skilled in the art would have believed at the time of filing (*In re Wright, 27 U5PQ2d 1510*). The state of the art indicates that very little is known about the humoral and, especially, cell-mediated immune response in pigs exposed to Lawsonia intracellularis. Pathogenesis of L. intracellularis has not been well investigated; however, organisms cultured in vitro have been used successfully to reproduce the disease in vivo. This bacterium has a tropism for intestinal epithelial cells, and the major pathological consequence of infection is hyperplasia of infected epithelial cells. The specific bacterial determinants, which confer pathogenicity and cause these distinctive pathological effects, are not known (see McCluskey et al, Infect Immun 2002 Jun; 70(6): 2899-907). Bacterial attachment and entry occur via the apical surface of immature epithelial cells in a process which appears to require a specific bacterial ligand-receptor interaction and once inside the cell, the bacteria escape from the vacuolar compartment into the cytoplasm, where they multiply and spread from cell to cell following cell division. At present, the determinants used by *L. intracellularis* to enter the cell, escape the vacuole, multiply intracytoplasmically, and modulate host cell function are not known. Therefore, the claimed outer-membrane protein induces an effective immune response such that it can be used, as a vaccine composition is not predictable in this underdeveloped art. The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for vaccine. In the absence of teachings that the claimed can generate a protective immune response, which is effective in preventing the infection or disease, the specification is not enabled for vaccines. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

Applicant states 5/2/05 that the claims 6, 7-21 and 23 are canceled and therefore the rejections are moot.

The examiner reviewed the amendment filed on 5/2/05 and noted claims 21 and 23 drawn to vaccine composition are pending. Therefore, the examiner disagrees with the applicant and maintaining the above rejection for claims 21 and 23.

Claim Rejections - 35 USC § 102 maintained

6. The rejection of claims 1-4, 21 and 23 under 35 U.S.C. 102(b) as being anticipated by McOrist et al, Infect Immun. 1989 March; 57 (3): 957–962 as evidenced by McOrist et al 1995 Int J Syst Bacteriol. 1995 Oct; 45(4): 820-5 is maintained as set forth in the previous office action.

The claims are now drawn to an isolated or recombinant immunogenic polypeptide comprising Lawsonia spp hemolysin polypeptide consisting of SEQ.ID.NO: 1 and a vaccine composition comprising said isolated polypeptide.

McOrist et al disclose an isolated protein profiles obtained with each Campylobacter species such as *C. mucosalis, C. hyointestinalis, C. jejuni*, C. *coli* and Campylobacter-like organism, also known as Lawsonia intracellularis (McOrist et al 1995). The prior art further identifies that the protein profile obtained from Campylobacter-like organism (see figure 1) was distinct and different from other species of Campylobacter such as *C. mucosalis, C. hyointestinalis, C. jejuni*, C. *coli.* This indicates that the intracellular Campylobacter-like organism (i.e., *L.intracellularis*) associated with proliferative enteropathy may be a novel bacterium with significant antigenic differences from the other Campylobacter species previously associated with the disease. Isoelectric focusing results suggested that Campylobacter like organisms in proliferate enteritis lesions possess a specific component of pI 4.5 (see in figure 4) with an antigenic site to that of the 25KD to 27KD (see figure 1) component detected in preparations in reducing gels. Therefore, it is likely that the components detected by the two methods represent the same structural component. Isoelectric focusing is a nondenaturing method, indicating that there is one major antigen and that the sodium dodecyl sulfate-polyacrylamide gel electrophoretic procedure denatures the antigen to 25-27kD. The absence of 25 to 27kD (PI 4.5) components in other *C. mucosalis, C. hyointestinalis, C. jejuni*, C. *coli* suggests that these organisms are antigenically different from known *C. mucosalis, C. hyointestinalis, C. jejuni*, C. *coli* and (see figure 4) and later studies recognized this Campylobacter-like organism as L.intracellularis.

The lower-molecular-weight OMP 25 KD to 27kD appears to be same as the claimed polypeptide comprising or consisting essentially of the amino acid sequence SEQ.ID.NO: 1. Therefore, 25 kD to 27kD protein is same as hemolysin polypeptide and thus read on the claimed invention. The isolated antigen migrating between 25kD- 27 kD on SDS-PAGE meet the limitations of the claimed polypeptide as recited in claims 1-4, 21 and 23 (figure 1) because

the disclosed 27kD antigen is from Lawsonia bacterium associated with proliferative enteropathy and in addition, such Campylobacter like organisms in proliferate enteritis lesions possess a specific component of pI 4.5 having 27kD protein and thus it reads on hemolysin (the broadly claimed having 251 amino acids is almost equivalent to 27kD of the prior art since each amino acid molecular weight is 110 daltons) polypeptide as claimed .

Thus, the prior art 27kD protein isolated from Lawsonia from pigs that have necrotic lesions with proliferative enteropathy is the "hemolysin" polypeptide of the claimed invention, and thus read on claimed polypeptide comprising the amino acid sequence SEQ.ID.NO: 1 because the claimed polypeptide having 251 amino acids is almost equivalent to 27kD protein of the prior art since each amino acid molecular weight is 110 daltons. It appears that applicant has cloned the DNA of the known hemolysin 27kD protein.

Since the isolated polypeptide obtained from pigs that have necrotic lesions with proliferative enteropathy, the said polypeptide reads on "hemolysin" polypeptide and it also reads on immunogenic as the polypeptide binds to antisera raised against sonicated Campylobacter-like organism (Lawsonia spp) as shown in figure 2. In the absence of evidence to the contrary that the disclosed polypeptide is immunogenic and showed strong reactions. Antisera to other Campylobacter species isolates did not react with preparations of intracellular organisms.

When producing an isolated 25-27kD protein as discussed above, the composition would inherently have a carrier present, i.e., buffer for pharmaceutical use as required by claim 21. Therefore, the composition comprising an isolated 25-27kD protein in buffer read on vaccine composition of claims 21, and 23.

In the absence of evidence to the contrary the disclosed prior art isolated polypeptide and composition and the claimed isolated and composition are the same. Since the Office does not have the facilities for examining and comparing applicants' claimed composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed composition and the composition of the prior art. It is acknowledged that weight is given to every term in claims. This is why the instant claims drawn to vaccine composition are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine compositions must be weighed with the structural limitations of the claim. If the vaccine composition merely comprises a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same composition as claimed.
In re Thorpe, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). In re Marosi, 218 U.S.P.Q. 289, 293-293 (C.A.F.C. 1983). In re Best, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). In re Brown, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972).

Applicants' arguments filed on 5/2/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that as a result of the amendment to the claims (an isolated or recombinant immunogenic polypeptide comprising Lawsonia spp hemolysin polypeptide

consisting of SEQ.ID.NO: 1 and a vaccine composition comprising said isolated polypeptide), the claimed invention is not anticipated by McOrist et al because the prior art does not disclose SEQ.ID.NO: 1

The examiner disagrees with the applicant because the newly amended claim "an isolated or recombinant immunogenic polypeptide comprising Lawsonia spp hemolysin polypeptide" (species of present and species that are going to be discovered) reads on the prior art polypeptide because the polypeptide disclosed is isolated and immnogenic comprising Lawsonia intracellularis 27kD hemolysin polypeptide. Applicant is claiming hemolysin polypeptide by sequence identification number and the disclosed hemolysin polypeptide is identified by molecular weight as stated above in the rejection. Therefore, applicant is advised to provide evidence indicating that the prior art protein is different from the claimed protein in structure, property or function.

New Claim Rejection - 35 USC 112, second paragraph based on the amendment

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as being vague for the recitation of " comprising Lawsonia spp hemolysin polypeptide consisting of SEQ.ID.NO: 1" It is not clear which polypeptide consist SEQ.ID.NO: 1? It is also not clear what else does an isolated or recombinant polypeptide comprise?

Remarks

9. No claims are allowed.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.